REMARKS

In the Office Action, the Examiner withdrew all rejections raised in the previous office action but raised a new written description rejection, a new enablement rejection, and a new lack of clarity rejection. Each new rejection is addressed separately below. In view of the amendments noted above and the remarks below, applicants respectfully request reconsideration of the merits of this patent application.

No extension of time is believed to be necessary and no fee is believed to be due in connection with this response. However, if any extension of time is required in this or any subsequent response, please consider this to be a petition for the appropriate extension and a request to charge the petition fee to Deposit Account No. 17-0055. No other fee is believed to be due in connection with this response. However, if any fee is due in this or any subsequent response, please charge the fee to the same Deposit Account No. 17-0055.

Written description rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 10, 14, and 42-49 as failing to comply with the written description requirement. In making the rejection, the Examiner first interpreted that claim language "an amino acid sequence selected from (i) amino acids 40-60 of SEQ ID NO:7 ... [and] (ii) amino acids 40-60 of SEQ ID NO:9 ..." to encompass a fragment of amino acids 40-60 of SEQ ID NO:7 or SEQ ID NO:9. In this regard, claims 10, 14, and 47 have been amended to recite the amino acid sequence selected from (i) the amino acids 40-60 of SEQ ID NO:7 and (ii) the amino acids 40-60 of SEQ ID NO:9. Applicants submit that the written description requirement for claims 14, 42-46, 48, and 49 as amended and new claim 68 is met.

Applicants also submit that the written description requirement for claims 10 and 47 as amended is met. Claims 10 and 17 as amended contain the additional subject matter of "(iii) the fragment of a mouse or rat synaptotagmin II homolog that corresponds to (i) or (ii)," i.e., the amino acids 40-60 of SEQ ID NO:7 or SEQ ID NO:9. Therefore, under (iii), applicants intend to cover the fragment of a synaptotagmin II protein from a species other than mouse or rat that corresponds to the amino acids 40-60 of SEQ ID NO:7 or SEQ ID NO:9.

To comply with the written description requirement, the specification only needs to describe in detail that which is new (*see Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d

1367 (Fed. Cir. 1986)). Regarding gene sequences in particular, the Federal Circuit has held that recitation of known gene sequences and essential regions or structures thereof is not required to meet the written description requirement.

In *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005), the court stated that "[t]he chimeric genes here at issue are prepared from known DNA sequences of known function. ... The Board erred in holding that the specifications do not meet the written description requirement because they do not reiterate the structure or formula or chemical name for the nucleotide sequences of the claimed chimeric genes."

In *Falko-Gunter Falkner v. Inglis,* 448 F.3d 1357 (Fed. Cir. 2006), the court rejected the petitioner's reliance on *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), for the proposition that the written description requirement was not met because Inglis did not describe "essential regions" of any poxvirus. "However, it is the binding precedent of this court that *Eli Lilly* does not set forth a *per se* rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art," the court noted.

The court further held that "a requirement that patentees recite known DNA structures, if one existed, would serve no goal of the written description requirement. ... Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly, we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences."

In the case of the present application, synaptotagmin II is a well known protein and the amino acid sequences of synaptotagmin II from a number of species are known and well conserved. The structure of synaptotagmin II is also conserved and well known in the art. For example, synaptotagmin II proteins from rat, mouse, and human are highly conserved (e.g., over 90% identical at the BoNT/B binding domain) and they all contain a luminal domain, a transmembrane domain, and a cytoplamic domain, which contains two C2 domains: C2A and C2B linked by a linker region (*see* paragraph [0007]).

What is new for the present invention is that the inventors pinpointed the BoNT/B binding domain of synaptotagmin II proteins through a series of structural and functional experiments (*see e.g.*, paragraphs [00067], [00068], [00071]-[00073], [00077], and [00078]). With the above new feature of the invention fully described in the specification and the synaptotagmin II proteins from a number of species well known in terms of their conserved amino acid sequences and structure, the written description requirement for "the fragment of a mouse or rat synaptotagmin II homolog that corresponds to the amino acids 40-60 of SEQ ID NO:7 or 9" is met. In this regard, the BoNT/B binding domain on a rat or mouse synaptotagmin II homolog can be readily recognized by a skilled artisan, for example by using an amino acid sequence alignment program (e.g., the widely used ClustalW web software at "http://www.ch.embnet.org/software/ClustalW.html" with the default settings) to identify the region that corresponds to the amino acids 40-60 of SEQ ID NO:7 or 9, especially given that the amino acid sequences and structures of synaptotagmin II proteins are highly conserved.

For all of the above reasons, it is respectfully submitted that the written description requirement for the claims as amended is met.

Enablement rejection under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 10, 14, and 42-49 as failing to meet the enablement requirement. In making the rejection, the Examiner first interpreted that claim language "an amino acid sequence selected from (i) amino acids 40-60 of SEQ ID NO:7 ... [and] (ii) amino acids 40-60 of SEQ ID NO:9 ..." to encompass a fragment of amino acids 40-60 of SEQ ID NO:7 or SEQ ID NO:9. In this regard, claims 10, 14, and 47 have been amended to recite the amino acid sequence selected from (i) the amino acids 40-60 of SEQ ID NO:7 and (ii) the amino acids 40-60 of SEQ ID NO:9. Applicants submit that the enablement requirement for claims 14, 42-46, 48, and 49 as amended and new claim 68 is met, as acknowledged by the Examiner in the office action (see page 9, Scope of Enablement, lines 2-10).

In addition, applicants have amended the subject matter of (iii) recited claims 14 and 47 to "(iii) the fragment of a mouse or rat synaptotagmin II homolog that corresponds to (i) or (ii)," i.e., the amino acids 40-60 of SEQ ID NO:7 or SEQ ID NO:9. As already discussed in detail above, synaptotagmin II is a well known protein with well conserved amino acid sequences and

structural/functional domains among different species. Therefore, with the disclosure in connection with the mouse and rat synaptotagmin II in the application, a skilled artisan appreciates that the fragment of a mouse or rat synaptotagmin II homolog from another species that corresponds to the amino acids 40-60 of the mouse or rat synaptotagmin II would also work. In this regard, applicants note the recent precedential opinion of *Ex parte Kubin* (Appeal 2007-0819) of the Board of Patent Appeals and Interferences (May 31, 2007) in which the Board held that a claim on "an isolated nucleic acid molecule comprising a polynucleotide encoding a polypeptide at least 80% identical amino acids 22-221 of SEQ ID NO:2, wherein the polypeptide binds CD48" is enabled even though the specification only provides a working example using sequence that encodes SEQ ID NO:2 and does not disclose which 20% of the amino acid residues should be changed to maintain the biological function of binding to CD48. The Board noted that the amount of experimentation to practice the full scope of the claimed invention might have been extensive, but it would have been routine and the techniques necessary to do so were well known to those skilled in the art. Similarly in the present application, some experiments might be necessary for testing whether the fragment of a mouse or rat synaptotagmin II homolog from another species that corresponds to the amino acids 40-60 of the mouse or rat synaptotagmin II would be able to form a complex with a ligand recited in the claims. However, such experiments are routine and the techniques to do so are well known to those skilled in the art. Therefore, claims 14 and 47 as amended are enabled.

For all of the above reasons, it is respectfully submitted that the enablement requirement for the claims as amended is met.

Indefiniteness rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claim 10 for failing to particularly point out and distinctively claim the subject matter of the invention. In particular, the Examiner pointed out that claim 10 states that the ligand is selected from BoNT/B and an antibody at one place but also states that the ligand is not a botulinum toxin at another place.

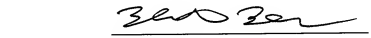
Applicants respectfully submit that claim 10 is definite in that when it states that "the ligand is not a botulinum toxin," it refers to the situation wherein the polypeptide is a full length synaptotagmin. In other words, when the polypeptide is not a full length synaptotagmin such as

the fragment of the amino acids 40-60 of the mouse or rat synaptotagmin II, the ligand can be BoNT/B. Claim 10 is clear in this regard. Withdrawal of the rejection is respectfully requested.

Summary

Having addressed each new rejection raised by the Examiner by claim amendments and arguments, the claims as amended are believed to be in condition for allowance and a Notice of Allowance is respectfully requested. Should any issues remain outstanding, the Examiner is invited to contact the undersigned at the telephone number appearing below if such would advance the prosecution of this application.

Respectfully submitted,



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